

REMARKS

Claim Amendments

Previously pending claims 29-44 are cancelled herewith without disclaimer or prejudice to prosecution of the subject matter of the claims in a related application. New claims 45-56 are added by this amendment. The new claims are directed to a method of preparing an epothilone D derivative with a methyl group at C-12 and a double bond between C-12 and C-13 by providing substrates including extender units to a non-*S. cellulosum* host cell that expresses a modified functional epothilone PKS with an epoD protein that lacks a β -carbonyl modifying activity. Support for the new claims is replete in the specification and claims as originally filed. Support for “a double bond between C-12 and C-13” in claim 45 is replete in the specification.¹ No new matter is believed to be added by the new claims.

It is submitted that the new *claims* are in condition for allowance. With regard to U.S. Pat. No. 6,355,459 (“Schupp”) cited by the Office in connection with the previously pending composition claims, Applicants submit the following observations:

The Schupp reference provides nucleotide sequence of the *Sorangium cellulosum* epothilone synthase gene cluster. However, the Schupp reference did not describe the compounds epothilone C or D and, moreover, erroneously taught that an exogenous (non-cluster) methyltransferase gene product is required to form epothilone B, the precursor of epothilone D, both of which are characterized by a methyl group at C-12. The Schupp reference contains no teaching or suggestion that the uncharacterized non-cluster methyltransferase gene was expressed in any non-*S. cellulosum* host cell. Nothing in the Schupp reference provided any expectation of success for producing an epothilone D derivative with a methyl group at C-12 and a double bond between C-12 and C-13 in a non-*S. cellulosum* host cell expressing a functional epothilone PKS with a modified EpoD protein.

¹ For example, at page 33, line 23, the specification explains that the C-12-C-13 alkene is a distinguishing characteristic of “epothilone D (*or an epothilone D derivative*)” [emphasis added]. As a further example, at page 16, line 22, the specification explains that epothilones C and D differ from epothilones A and B because “they lack the C-13 hydroxyl and have a double bond between C-12 and C-13.”

The present inventors described the synthesis of epothilone D and provided specific guidance about the results of particular modifications of the epoD gene (see, *e.g.*, pages 31-41 of the specification). The present inventors thus provided motivation *not found* in the Schupp reference to produce an epothilone D derivative in a non-*S. cellulorum* host cell and, further, provides an expectation of success *not found* in the Schupp references that epothilone D derivatives with a methyl group at C-12 and a double bond between C-12 and C-13 could be produced in a non-*S. cellulorum* host cell.

CONCLUSION

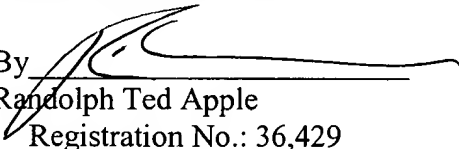
In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

Applicants have, by way of the amendments and remarks presented herein addressed all issues that were raised in the outstanding Office Action. Applicants respectfully submit that this Amendment has demonstrated there is no legal basis for the rejections and so that the pending claims are in condition for allowance. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 300622003110. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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